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Pesticide Fact Sheet Number 204: Triadimenol (Baytan)

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This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

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United States
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Office of Pesticides
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540/FS-89-058

EPA

Pesticide Fact Sheet

Name of Chemical: beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol

Reason for Issuance: New Chemical Registration

Date Issued: July 1989

Fact Sheet Number: 204

DESCRIPTION OF CHEMICAL

Generic Name: beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol and its metabolites containing chlorophenoxy and triazole moieties.

Common Name: triadimenol

Trade Name: Baytan

EPA Shaughnessy Codes: 127201

Chemical Abstracts Service (CAS) Number: 5219-65-3

Year of Initial Registration: 1989

Pesticide Type: Fungicide

U.S. and Foreign Producers: Mobay Corporation

USE PATTERNS AND FORMULATIONS

APPLICATION SITES: Seeds of barley, corn, oats, rye, sorghum and wheat to control seed- and soil-borne diseases and to provide early season control of foliar diseases.

METHOD OF APPLICATION: Application will be made as a water-based slurry through standard slurry or mist type commercial seed treatment equipment.

TYPES OF FORMULATION: 25% dry flowable end-use product and 90% technical powder for formulating use.

APPLICATION RATES: For barley, oats, rye and wheat, apply 0.25-0.5 oz. ai./100 lbs of seed; for sorghum, apply 0.5 oz. ai./100 lbs of seed; and for corn, apply 1.0 oz.-ai./100 lbs of seed.

USUAL CARRIER: water.

SCIENCE FINDINGS

Summary Science Statement

Available acute toxicity studies indicate that triadimenol is in toxicity category II (warning) based on an acute inhalation toxicity study with rats.

Chronic feeding/oncogenicity studies were conducted in both the rat and mouse. Clinical chemistry findings in the chronic feeding study in the rat suggests that the target organ for toxicity may be the liver. Although there was an accompaying small increase in liver weight in the females of the high dose group, there were no histopathologic charges in the liver in either sex.

In the chronic feeding study in mice, the results of blood chemistry, organ weights and gross and histological examinations, again indicated the liver as the target organ.

Triadimenol did not induce either genotoxic effects or chromosomal aberrations in a series of mutagenicity studies. In addition, no strong structural activity correlation to other carcinogens has been found. Triadimenol was also found not to be teratogenic in either the rat or rabbit.

Environmental fate data indicates that triadimenol is stable to hydrolysis and appears to be stable to photolysis on the soil surface. In addition, based on low adsorption coefficients, triadimenol will have a low potential to leach in soil. However, triadimenol may have a moderate potential to leach in some Western soils.

Additional studies indicate that due to the manufacturing process, triadimenol should have no adverse effects on non-target organisms provided waste is disposed of properly. An overview of the toxicity test results suggests that triadimenol is practically non-toxic to birds, slightly toxic to fish, and moderately toxic to aquatic invertebrates. It is also unlikely that this registration would affect endangered species because of its relatively low use rates, agricultural techniques which involve drill planting of most small grains and corn, and the low toxicity of triadimenol to all animals.

TOXICOLOGICAL CHARACTERISTICS

Acute oral toxicity in rats:
LD_{50} 689 mg/kg in males
752 mg/kg in females
Toxicity category III

Acute dermal toxicity in rats:
LD_{50} >5000 mg/kg
Toxicity category III

Acute inhalation toxicity in rats
LC_{50} >1.56 mg/L
Toxicity category III

Primary eye irritation in rabbit:
slight irritation

Primary dermal irritation in rabbit:
Toxicity category IV

Dermal sensitization in guinea pigs:
core minimum; no effect

Chronic Studies: Triadimenol has been evaluated in the following studies.

°Rodent Feeding/Oncogenicity

1. A 2-year feeding/oncogenicity study with rats using dietary concentrations of 0, 125, 500, and 2000 parts per million (ppm) equivalent to 0, 6.25, 25.0, and 100 mg/kg bwt/day in males and females. Clinical chemistry findings suggest that the target organ for toxicity may be the liver. The levels of SGOT and SGPT enzymes were consistently higher at 2000 ppm in males and females when compared to controls, and some increase in these two parameters was also observed at 500 ppm. Although there was an accompanying small increase in liver weight in 2000 ppm females, there were no accompanying increases in histopathologic changes of the liver in either sex. There were only marginal effects seen on other clinical chemistry parameters, and no effect of test compound on clinically observed signs of toxicity, food consumption, hematologic, or urinalysis parameters. The systemic NOEL (no-observed effect level) is 125 ppm (6.25 mg/kg/day for males and females) based on the increase in liver enzymes (SGOT and SGPT). The systemic LEL (lowest effect level) was 500 ppm (25 mg/kg/day for males and for females).

2. A 2-year chronic feeding/oncogenicity study in mice using dietary concentrations of 0, 125, 500, and 2000 ppm (equivalent to doses of 0, 18, 72, and 285 mg/kg/day for males and females). The results of blood chemistry, organ weights, and gross and histological examinations indicated the liver to be the target organ. There were time- and dose-related increases in SAP (serum alkaline phosphatase), SGOT and SGPT activities in both male and female animals receiving 500 and 2,000 ppm of the test material.

In addition, increased incidence of enlarged livers, hyperplastic nodules and increased liver weights in both male and female animals receiving 2,000 ppm of test material were detected at necropsy. Female animals receiving 2000 ppm exhibited a significant increase in the incidences of liver adenomas only, a compound-related oncogenic effect. In

males, there were no differences in the incidences of these lesions in treated and control males, and the incidences of liver adenomas were similar to those observed in historical controls.

Based on this evidence the Agency classified triadimenol as a Category C (possible human carcinogen) in accordance with the EPA Guidelines for Carcinogen Risk Assessment (September 24, 1986, 51 FR 33992). This evaluation was confirmed by the Agency's Scientific Advisory Panel on December 15, 1987. However, it was also concluded that this evidence of carcinogenicity did not warrant a low dose extrapolation of risks since the tumors were only benign, were observed in only one sex, and only at the highest dose tested. Moreover, the chemical was negative in the genotoxic assay battery.

Based on blood chemistry findings, the systemic NOEL and the LEL are 125 ppm and 500 ppm respectively (equivalent to 18 and 72 mg/kg/day for males and females).

3. A 3-month rat feeding study using doses of 0, 150, and 600 ppm (equivalent to 0, 7.5, and 30 mg/kg bwt/day for males and females) demonstrated a decrease in body weight, decrease in hematocrit values, eosinophil count and medium cell hemoglobin and increase in the high dose group and dose-related increase in liver weight. The NOEL is 150 ppm and the LEL is 600 ppm.

°Non-Rodent Feeding Study

1. A 2-year male and female dog feeding study using doses of 0, 150, 600 and 2400 ppm (equivalent to 0, 3.75, 15, and 60 mg/kg bwt/day for males and females). The NOEL is 150 ppm based on changes in enzyme levels (equivalent to 3.75 mg/kg bwt/day for males and females). The LEL is 600 ppm. Although there were significant decreases in mean body weights in males receiving 150 and 2400 ppm and in females receiving 600 and 2400 ppm, the biological significance of these changes could not be assessed. There were noted increases in alkaline phosphatase N-demethylase, and cytochrome P-450 in males receiving 2400 ppm and significant increases in N-demethylase in females receiving 600 and 2400 ppm and in cytochrome P-450 in females receiving 2400 ppm when compared to controls.

2. A 6-month dog feeding study using doses of 0, 10, 30, and 100 ppm (equivalent to 0, 0.25, 0.75, 2.5 mg/kg bwt/day for males and females). The NOEL was demonstrated at doses up to 100 ppm, the highest dose level tested.

3. A 3-month dog feeding study using doses of 0, 150, 600 and 2400 ppm (equivalent to 0, 3.75, 15, and 60 mg/kg bwt/day for males and females). Weight gain in all male groups and in the highest dose female group was significantly less than the control. Alkaline phosphatase in males and females showed a dose-related negative trend. There was no gross pathological changes. Effects at 600 ppm included an increase in serum cholesterol level in males. Although the NOEL appeared to be

less than 150 ppm based on reduced body weight and decreased alkaline phosphatase in males, the Agency has concluded that effects below 600 ppm in the 2-year dog study were not biologically significant and the longer-term study supercedes the 90-day dog study. Therefore, the NOEL remains at 150 ppm.

°Teratology

1. A rabbit teratology study with a NOEL for maternal toxicity of 8 mg/kg. The maternal LEL was 40 mg/kg based on decreased body weight gains and food consumption. The developmental NOEL and LEL were 40 mg/kg and 200 mg/kg respectively. This study has to be resubmitted with all the findings statistically analyzed on a per litter and per fetus basis in order to be upgraded from its current classification as core supplementary.

2. A rat teratology study using dose levels 0, 30, 60, and 120 mg/kg/day was determined to be core supplementary because the NOEL for developmental toxicity (supernumerary ribs) was not definitively established. The NOEL and LOEL for maternal toxicity for this study are 30 and 60 mg/kg/day, respectively, based on decreases in maternal body weight, body weight gain, and food consumption at 60 and 120 mg/kg/day. Furthermore, increased embryolethality (embryotoxicity) was only observed at the highest dose level tested (120 mg/kg/day). This study must be repeated to clearly define a NOEL for developmental toxicity.

The above rat study indicated that triadimenol caused a dose-dependent, statistically significant increase in the incidence of rudimentary supernumerary ribs. Although the effect at the low dose level was not statistically significant, it was considered to be treatment related because of the dose-related trend.

The biological significance of the manifestation of supernumerary ribs is subject to scientific debate, especially if the ribs are not fully developed (rudimentary). Nonetheless, the margin of safety (MOS) for this effect must be taken into consideration. The MOS is the ratio between the NOEL for the effect and the acute exposure in mg/kg/day. A NOEL for developmental toxicity could not be defined in the rat teratology study but it is unlikely to be far below the threshold (LEL) of 30 mg/kg/day observed in the current study.

Based on worker exposure information and an estimation of the NOEL at about 15 mg/kg/day for developmental toxicity (rudimentary supernumerary ribs in rats) and assuming a maximum dermal penetration of about 10%, a margin of safety was calculated to be >100 for factory workers involved in seed treatments using a closed system. Because of possible developmental toxicity and the lack of a will defined NOEL for this effect, the product label must include a recommendation for the use of protective clothing by factory workers involved in the treatment of seeds and for farm workers handling the treated seed.

°Reproduction.

A rat multigeneration reproduction study using doses of 0, 20, 100, and 500 ppm (equivalent to 0, 1, 5, and 25 mg/kg bwt/day for males and females) indicated that the NOEL and LOEL for both parental and pup toxicity are 100 and 500 ppm, respectively, based on significant body weight and organ weight changes. The NOEL for reproductive toxicity is 500 ppm, highest dose level tested.

°Mutagenicity:

A reverse mutation assay (AMES), a dominant lethal test in mice, DNA damage/repair, unscheduled DNA synthesis, in vitro and in vivo (rat) cytogenic assays, and a forward mutation in mice, all of which were negative for mutagenic effects.

ENVIRONMENTAL FATE

Hydrolysis: STABLE. Triadimenol in sterile aqueous buffer solutions showed no apparent degradation at either temperature or pH tested. Recovery was 97% greater after 32 days of incubation.

Soil Surface Photolysis: STABLE. Triadimenol appears to be stable to photolysis on the soil surface. Studies indicate that triadimenol photodegrades with a half-life of 36 hours in distilled water and 17 hours in a photo-sensitized (acetone) solution.

Aerobic Soil Metabolism: STABLE. Studies indicate that triadimenol has an estimated aerobic half-life of 8 to 9 months. Triadimenol reached a maximum level of 68% of that applied at 14C in 71 days and declined slightly to 45.2% by day 238. Consequently, the anaerobic half-life is considerably greater than 8-9 months.

Adsorption/Desorption: Because of its low adsorption coefficients, triadimenol is shown to have a low to moderate potential to bind to soil particles. Studies indicate that the adsorption coefficient, k, for triadimenol ranged from 2.37 to 5.26. The k values for desorption ranged from 1.49 in a silty clay soil (0.49 ppm) to 9.12 in a loam soil (9.57 ppm). Consequently, there is no correlation between adsorption and soil organic matter content. The highest

degree of adsorption was observed with the loam soil, intermediate in organic matter content.

Environmental fate data requirements have been satisfied with the exception of a field dissipation study. The company will be required to submit results of this study by July 1990.

ECOLOGICAL CHARACTERISTICS

Studies submitted show that this chemical is practically non-toxic to birds, slightly toxic to fish and moderately toxic to aquatic invertebrates. It is unlikely that the seed treatment use of triadimenol will affect any terrestrial or aquatic animals. Chronic effects are unlikely due to the low use rates and because the seed treatment use requires incorporation of seeds into the soil. For the above reasons it is also unlikely that this use will affect any endangered species.

BENEFITS

This chemical has been shown to be environmentally safe, is used at low rates and has a broad biological spectrum. Triadimenol controls seed-, soil-, and wind-borne pathogens of wheat, barley, oats, rye, corn and sorghum. Crops may be grazed 40 days after seeding. The chemical improves winter survival and drought tolerance of cereals, lowers the inoculum levels for overwintering foliar diseases and may eliminate the need for early season foliar sprays.

TOLERANCE ASSESSMENT:

Tolerances are established for the fungicide triadimenol and its butanediol metabolite (calculated as triadimenol) in or on the following commodities: 2.5 ppm for green forage of barley, oats, rye and wheat; 0.1 ppm for straw of barley, oats, rye and wheat; 0.05 ppm for grains of barley, oats, rye and wheat, corn fodder, fresh corn (including sweet), corn forage, corn grain, and green forage of sorghum; and 0.01 ppm for sorghum grain and sorghum fodder. Tolerances are established for the fungicide triadimenol and its metabolites containing the chlorophenoxy moiety (calculated as triadimenol) in or on the following commodities: 0.1 ppm for fat, meat and meat by-products of cattle, goats, hogs, horses, and sheep; and 1.01 ppm for eggs, milk, and fat, meat and meat by-products of poultry.

Where tolerances are established for residues of both 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone (triadimefon) and triadimenol, including its butanediol metabolite,

in or on the same raw agricultural commodity and its products thereof, the total amount of such residues shall not yield more residue than that permitted by the higher of the two tolerances. The nature of the residue is adequately understood and the Agency concluded that the pesticide is useful for the purposes for which tolerances are sought and that the establishment of the tolerances will protect the public health.

SUMMARY OF MAJOR DATA GAPS:

The Agency concurs with conditional registration of this chemical for use as a seed treatment fungicide pending submission of a field dissipation study by July 1990.

CONTACT PERSON AT EPA

Susan T. Lewis,
Acting Product Manager (PM) 21,
Registration Division (H-7505C),
Environmental Protection Agency,
401 M St., SW.,
Washington, DC 20460

Office location and telephone number:
Rm. 227, CM#2,
1921 Jefferson Davis Highway,
Arlington, VA 22202
(703) 557-1900

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